

STUDIES ON THE PRODUCTION OF
ANTIBIOTICS BY YEASTS

BY
WINIFRED RUTH MITCHELL

B. S., University of Illinois, 1941

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AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN BACTERIOLOGY
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The discovery of penicillin as a valuable chemotherapeutic agent has stimulated investigations into the production of similar compounds by other organisms. Although considerable work has been done to determine whether or not fungi produce substances inimical to bacteria, little has been done with yeasts. Some genera of the higher fungi, Ascomycetes, and Schizomycetes are known to produce bacteriostatic and bactericidal agents. As many yeasts are Ascomycetes and many are phylogenetically related to the higher fungi as well as to the Schizomycetes, one might expect them to produce agents with characteristics comparable to those exhibited by penicillin. The object of the present research was to determine whether or not certain species of yeasts do synthesize substances similar to penicillin, substances which have an inhibitive effect on bacteria.

The word *antibiotic*, although defined variously by its users, has been limited in this instance to mean compounds, formed by organisms, which are capable of inhibiting the cell multiplication of micro-organisms.

Groups of fungi have been studied for the production of antibiotic compounds (22, 17, 14), and compounds have been isolated from cultures of *Penicillia* (6, 3), *Aspergilli* (16), *Fusaria* (1), *Pseudomonas* (19, 10), *Streptomyces* (21, 5), and *Bacilli* (12, 13, 15) to name a few.

Brocq in 1899 stated beer yeasts had been used as a remedy for boils for years. There are numerous references throughout the literature to the effectiveness of various yeast preparations for topical application, some of which were reviewed by Durand (8). Fernbach (9) was the first to isolate a compound from pure culture yeasts, in this case an amine, with antibacterial activity. Bachmann and Ogait (2) identified acetaldehyde from yeast cultures and found it to have antibacterial action. Cook, *et al.*, (7) purified a substance from baker's yeast which had antifungal activity. Takahashi (20) isolated a polysaccharide from yeast cakes and found it to be a virus depressant. Carpenter (4) reported that *Torulopsis utilis* variety *major* and *thermophila* produced

a non-volatile acid with antibacterial activity. Recently, Sartory (18) obtained a material from a *Debaromyces* and from baker's yeast with antibiotic activity.

In the present investigation, 229 yeasts were tested for antibiotics on a 0.1 per cent glucose, nutrient agar medium. One hundred and sixteen were from the collection of the University of Illinois, 38 were from the Northern Regional Research Laboratory, and 75 were isolations from nature. The yeasts were grown on one side of the medium in petri plates, and after five days incubation, were tested by streaking *Escherichia coli*, *Bacillus subtilis*, and *Staphylococcus aureus* into the yeast growth. These were observed for the absence of visible growth adjacent to the yeast growth. By this test none of the yeasts were found to produce antibiotics, whereas 17 out of 19 spore-forming rods tested did inhibit at least one of the test organisms. Known antibiotic-producing organisms, such as *Streptomyces griseus* (21), *Penicillium notatum* (6), *Bacillus brevis* (12), *Bacillus subtilis* (13), *Aspergillus fumigatus* (16), and *Aspergillus clavatus* (3), gave inhibition of at least one test organism by this method.

Forty-four species of yeasts were grown in three different media, one of which contained steep water, another tryptone, and the third semi-synthetic nutrients. The cultures were grown under conditions of aeration. These were tested for antibiotic activity against fifteen bacteria, most of which were pathogens. When the solutions were neutralized, there was no antibiotic activity.

In another experiment eight species of yeasts produced no antibiotic activity when grown on several media, including one containing ten per cent glucose, when the solutions were neutralized before testing.

Disintegrated cells from sixteen species of yeasts did not give positive antibiotic tests. Eight species were tested for non-diffusible antibiotics by using *Staphylococcus aureus* in a liquid medium with negative results.

When the yeasts were tested on a 0.5 per cent glucose agar medium by the streak plate method *Schizosaccharomyces*

pombe (*Schizosaccharomyces mellacei*) and *Klockera brevis* inhibited the test organisms. When grown in a two per cent glucose medium under submerged conditions, *Schizosaccharomyces pombe* was found to produce a volatile acid which gave zones of inhibition on the filter pad antibiotic plate test. Neutralized samples and neutralized distillate gave no antibiotic test. When fermented liquor from *Klockera brevis* was tested, un-neutralized samples gave a positive test, whereas the neutralized did not.

In the foregoing experiments a number of the yeasts were shown to produce positive antibiotic tests when the solution was not neutralized. However, upon neutralization the antibiotic activity disappeared.

None of the yeasts tested under our conditions showed antibiotic activity other than inhibition due to acids.

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The author is a member of the Society of American Bacteriologists, American Association for the Advancement of Science, American Chemical Society, Sigma Xi, and Phi Sigma. Publications are as follows:

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Patents:

Two applications of Tyrothricin fermentation by Commercial Solvents Corporation.



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